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Patent

IN THE CLAIMS

Please amend claim 1 to read as follows:

1. (Amended) A compound of formula

wherein:

R₁ is hydrogen, aryl, heteroaryl, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, or C5-C8-cycloheteroalkyl having from 1-2 heteroatoms selected from N, NR₇, S and O; R₂ and R₃ are each independently, hydrogen, alkyl of 1-6 carbon atoms, -CN, or -CCH; R₅is hydrogen, alkyl of 1-8 carbon atoms, cycloalkyl of 3-6 carbon atoms, aryl, heteroaryl, or C4-C8-cycloheteralkyl;

 R_7 is hydrogen, aryl, aralkyl, alkyl of 1-6 carbon atoms, or cycloalkyl of 3-6 carbon atoms, oxy, C1-C8 alkanoyl, COOR₅, COR₅, -SO₂-C1-C8 alkyl, -SO₂-aryl, -SO₂-heteroaryl, -CO-NHR₁;

R₈, R₉, R₁₀, and R₁₁ are each, independently, hydrogen, aryl, aralkyl, 5-10 membered heteroaryl having from 1-3 heteroatoms selected from N, NR₇, O and S, heteroaralkyl having from 1-3 heteroatoms selected from N, NR₇, O and S, cycloalkyl of 3-6 carbon atoms, -C4-C8-cycloheteroalkyl having from 1-3 heteroatoms selected from N, NR₇, O and S, alkyl of 1-18 carbon atoms, alkenyl of 2-18 carbon atoms, alkynyl of 2-18 carbon atoms;

R₁₂ is hydrogen, aryl or 5-10 membered heteroaryl having from 1-3 heteroatoms selected from N, NR₇, S and O, cycloalkyl of 3-6 carbon atoms, -C₅-C₈-cycloheteroalkyl having from 1 to 2 heteroatoms selected from N, NR₇, S and O, or alkyl of 1-6 carbon atoms;

A is O, S, SO, SO₂, NR₇, or CH₂;

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X is O, S, SO, SO₂, NR₇, or CH₂;

Y is aryl or heteroaryl, with the proviso that A and X are not bonded to adjacent atoms of Y and with the further proviso that Y is not phenyl; and

n is 0-2; or a pharmaceutically acceptable salt thereof.

Please amend claim 2 to read as follows:

2. (Amended) A compound according to claim 1 wherein Y is pyridyl, thienyl, furanyl, imidazolyl, triazolyl, or thiadiazolyl.

Please amend claim 5 to read as follows:

5. (Amended) A method of inhibiting pathological changes mediated by TNF- α converting enzyme (TACE) in a mammal in need thereof which comprises administering to said mammal a therapeutically effective amount of a compound having the formula:

$$R_2$$
 R_3
 R_8
 R_{10}
 R_{11}
 R_{11}
 R_{12}

wherein:

R₁ is hydrogen, aryl, heteroaryl, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, or C₅-C₈-cycloheteroalkyl having from 1-2 heteroatoms selected from N, NR₇, S and O;

R₂ and R₃ are each independently, hydrogen, alkyl of 1-6 carbon atoms, -CN, or -CCH;

R₅is hydrogen, alkyl of 1-8 carbon atoms, cycloalkyl of 3-6 carbon atoms, aryl, heteroaryl, or C4-C8-cycloheteralkyl;

R₇is hydrogen, aryl, aralkyl, alkyl of 1-6 carbon atoms, or cycloalkyl of 3-6 carbon atoms, oxy, C1-C8 alkanoyl, COOR₅, COR₅, -SO₂-C1-C8 alkyl, -SO₂-aryl, -SO₂-heteroaryl, -CO-NHR₁;

R₈, R₉, R₁₀, and R₁₁ are each, independently, hydrogen, aryl, aralkyl, 5-10 membered heteroaryl having from 1-3 heteroatoms selected from N, NR₇, O and S, heteroaralkyl having from 1-3 heteroatoms selected from N, NR₇, O and S, cycloalkyl of 3-6 carbon atoms, -C4-C8-cycloheteroalkyl having from 1-3 heteroatoms selected from N, NR₇,

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O and S, alkyl of 1-18 carbon atoms, alkenyl of 2-18 carbon atoms, alkynyl of 2-18 carbon atoms;

R₁₂ is hydrogen, aryl or 5-10 membered heteroaryl having from 1-3 heteroatoms selected from N, NR₇, S and O, cycloalkyl of 3-6 carbon atoms, -C5-C8-cycloheteroalkyl having from 1 to 2 heteroatoms selected from N, NR₇, S and O, or alkyl of 1-6 carbon atoms;

A is O, S, SO, SO₂, NR₇, or CH₂;

X is O, S, SO, SO₂, NR₇, or CH₂;

Y is aryl or heteroaryl, with the proviso that A and X are not bonded to adjacent atoms of Y and with the further proviso that Y is not phenyl; and

n is 0-2; or a pharmaceutically acceptable salt thereof.

Please amend claim 7 to read as follows:

7. (Amended) A pharmaceutical composition comprising a compound having the formula:

wherein:

R₁ is hydrogen, aryl, heteroaryl, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, or C5-C8-cycloheteroalkyl having from 1-2 heteroatoms selected from N, NR₇, S and O;

R₂ and R₃ are each independently, hydrogen, alkyl of 1-6 carbon atoms, -CN, or -CCH;

R₅is hydrogen, alkyl of 1-8 carbon atoms, cycloalkyl of 3-6 carbon atoms, aryl, heteroaryl, or C4-C8-cycloheteralkyl;

R₇is hydrogen, aryl, aralkyl, alkyl of 1-6 carbon atoms, or cycloalkyl of 3-6 carbon atoms, oxy, C1-C8 alkanoyl, COOR₅, COR₅, -SO₂-C1-C8 alkyl, -SO₂-aryl, -SO₂-heteroaryl, -CO-NHR₁;

R₈, R₉, R₁₀, and R₁₁ are each, independently, hydrogen, aryl, aralkyl, 5-10 membered heteroaryl having from 1-3 heteroatoms selected from N, NR7, O and S, heteroaralkyl